

What is claimed is:

1. A pharmaceutical agent delivery composition comprising:

a transport polymer comprising a peptide, characterized as having at least 10 amino acid residues, and wherein at least 10% of said amino acid residues are histidine, and wherein the molecular structure of

5 said peptide is selected from the group consisting of:

linear, with the proviso that:

a. the entire sequence of said peptide cannot be described by the formula:  $(XHHX)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4;

10 b. the entire sequence of said peptide cannot be described by the formula:  $(XHXH)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4; and

c. said peptide does not comprise a hexa-peptide having the sequence

His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of  
15 said peptide are histidine; and

branched, with a backbone peptide of 1 or more amino acid residues and at least one peptide branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone peptide, with the proviso that each peptide branch can consist of a single histidine residue only if the backbone peptide does not consist  
20 solely of lysine residues; and

a pharmaceutical agent associated with said transport polymer.

2. The pharmaceutical agent delivery composition of claim 1, wherein at least 25% of the amino acid residues of said peptide are histidine.

3. The pharmaceutical agent delivery composition of claim 1, wherein said peptide comprises a  
25 subsegment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),

K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),

K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),

5 K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),

K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),

K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),

H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),

K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),

10 end-to-end repeats of one or more of the above sequences, and

the reverse of any of the above sequences.

4. The pharmaceutical agent delivery composition of claim 1, further comprising at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

5. The pharmaceutical agent delivery composition of claim 4, wherein said intracellular delivery component comprises a lipid.

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6. The pharmaceutical agent delivery composition of claim 1, further comprising a transition metal.

7. The pharmaceutical agent delivery composition of claim 1, wherein said pharmaceutical agent consists of at least one therapeutic agent.

8. The pharmaceutical agent delivery composition of claim 7, wherein said therapeutic agent is selected from the group consisting of a protein, an oligopeptide, a nucleic acid, a cancer chemotherapeutic agent, an infectious disease chemotherapeutic agent, and any combination of two or more of the above.

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9. The pharmaceutical agent delivery composition of claim 8, wherein said therapeutic agent is nucleic acid.

10. The pharmaceutical agent delivery composition of claim 9, wherein said nucleic acid is an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, or a combination of two or more of the above.

11. The pharmaceutical agent delivery composition of claim 1, wherein at least 10% of the non-histidine amino acid residues of said peptide carry a positive charge at physiological pH.

12. A method for delivering a pharmaceutical agent to the interior of a cell, said method comprising a step of contacting the cell with the pharmaceutical agent delivery composition of claim 1.

13. The method of claim 12, wherein the molecular structure of said peptide is branched.

14. The method of claim 12, wherein said peptide comprises a subsegment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),

K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),

K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),

K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),

K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),

H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),

K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),

end-to-end repeats of one or more of the above sequences, and

the reverse of any of the above sequences.

15. The method of claim 12, wherein said pharmaceutical agent delivery composition further comprises at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

16. The method of claim 15, wherein said intracellular delivery component comprises a lipid.

17. The method of claim 12, wherein said pharmaceutical agent delivery composition further comprises a transition metal.

18. The method of claim 12, wherein said pharmaceutical agent consists of at least one therapeutic  
5 agent.

19. The method of claim 18, wherein said therapeutic agent is selected from the group consisting of a protein, an oligopeptide, a nucleic acid, a cancer chemotherapeutic agent, an infectious disease chemotherapeutic agent, and any combination of two or more of the above.

20. The method of claim 19, wherein said therapeutic agent is nucleic acid.

10 21. The method of claim 20, wherein said nucleic acid is an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, or a combination of two or more of the above.

22. The method of claim 12, wherein at least 10% of the non-histidine amino acid residues of said peptide carry a positive charge at physiological pH.

23. The method of claim 12, further comprising the steps of:

15 removing said cell from a subject prior to contacting said cell with said pharmaceutical agent delivery composition; and  
administering said cell to said subject after contacting said cell with said pharmaceutical agent delivery composition.

20 24. The method of claim 23, wherein said pharmaceutical agent delivery composition further comprises an intracellular delivery component.

25. A method for producing a pharmaceutical agent delivery composition comprising the steps of:

- a. providing a transport polymer comprising a peptide characterized as having at least 10 amino acid residues, and wherein at least 10% of said amino acid residues are histidine, and wherein the molecular structure of said peptide is selected from the group consisting of:

linear, with the proviso that:

- i. the entire sequence of said peptide cannot be described by the formula:  $(XHHX)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4;
- ii. the entire sequence of said peptide cannot be described by the formula:  $(XHXH)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4; and

- iii. said peptide does not comprise a sequence His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of said peptide are histidine; and

branched, with a backbone peptide of 1 or more amino acid residues and at least one peptide branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone peptide, with the proviso that each peptide branch can consist of a

single histidine residue only if the backbone peptide does not consist solely of lysine residues;

- b. providing a pharmaceutical agent capable of associating with said transport polymer;
- c. combining said transport polymer with said pharmaceutical agent to form a polymer/pharmaceutical agent complex; and
- d. mixing said complex with an intracellular delivery component.

26. The method of claim 25, wherein said intracellular delivery component comprises a lipid.